acid. For example, huTNF-RΔ235 refers to human TNF-R having Asp^{235} as the C-terminal amino acid (i.e., a polypeptide having the sequence of amino acids 1-235 of [~~Figure~~ FIG. 2A] SEQ ID NO:1). In the absence of any human or murine species designation, TNF-R refers generically to mammalian TNF-R. Similarly, in the absence of any specific designation for deletion mutants, the term TNF-R means all forms of TNF-R, including mutants and analogs which posses TNF-R biological activity. --

Page 6, lines 1-21, delete in their entirety, and insert therefor

-- "Soluble TNF-R" or "sTNF-R" as used in the context of the present invention refer to proteins, or substantially equivalent analogs, having an amino acid sequence corresponding to all or part of the extracellular region of a native TNF-R, for example, huTNF-RΔ235, huTNF-RΔ185 and huTNF-RΔ163, or amino acid sequences substantially similar to the sequences of amino acids 1-163, amino acids 1-185, or amino acids 1-235 of [~~Figure~~ FIG. 2A] SEQ ID NO:1, and which are biologically active in that they bind to TNF ligand. Equivalent soluble TNF-Rs include polypeptides which vary from these sequences by one or more substitutions, deletions, or additions, and which retain the ability to bind TNF or inhibit TNF signal transduction activity via cell surface bound TNF receptor proteins, for example huTNF-RΔx, wherein x is selected from the group consisting of any one of amino acids 163-235 of [~~Figure~~ FIG. 2A] SEQ ID NO:1. Analogous deletions may be made to muTNF-R. Inhibition of TNF signal transduction activity can be determined by transfecting cells with recombinant TNF-R DNAs to obtain recombinant receptor expression. The cells are then contacted

with TNF and the resulting metabolic effects examined. If an effect results which is attributable to the action of the ligand, then the recombinant receptor has signal transduction activity. Exemplary procedures for determining whether a polypeptide has signal transduction activity are disclosed by Idzerda et al., *J. Exp. Med.* *171*:861 (1990); Curtis et al., *Proc. Natl. Acad. Sci. USA* *86*:3045 (1989); Prywes et al., *EMBO J.* 5:2179 (1986) and Chou et al., *J. Biol. Chem.* *262*:1842 (1987). Alternatively, primary cells or cell lines which express an endogenous TNF receptor and have a detectable biological response to TNF could also be utilized. --

Page 8, lines 16-28 delete in their entirety, and insert therefor

-- The coding sequence of TNF-R is obtained by isolating a complementary DNA (cDNA) sequence encoding TNF-R from a recombinant cDNA or genomic DNA library. A cDNA library is preferably constructed by obtaining polyadenylated mRNA from a particular cell line which expresses a mammalian TNF-R, for example, the human fibroblast cell line WI-26 VA4 (ATCC CCL 95.1) and using the mRNA as a template for synthesizing double stranded cDNA. The double stranded cDNA is then packaged into a recombinant vector, which is introduced into an appropriate *E. coli* strain and propagated. Murine or other mammalian cell lines which express TNF-R may also be used. TNF-R sequences contained in the cDNA library can be readily identified by screening the library with an appropriate nucleic acid probe which is capable of hybridizing with TNF-R cDNA. Alternatively, DNAs encoding TNF-R proteins can be assembled by ligation of synthetic

oligonucleotide subunits corresponding to all or part of the sequence of [~~Figures~~ FIGS. 2-3 or ~~Figures~~ FIGS. 4-6] SEQ ID NO:1 or SEQ ID NO:3 to provide a complete coding sequence. --

Page 9, lines 20-26, delete in their entirety, and insert therefor

-- Using this approach, approximately 240,000 cDNAs were screened in pools of approximately 800 cDNAs until assay of one transfectant pool indicated positive foci for TNF binding. A frozen stock of bacteria from this positive pool was grown in culture and plated to provide individual colonies, which were screened until a single clone ([clone 11] clone 1) was identified which was capable of directing synthesis of a surface protein with detectable TNF binding activity. The sequence of cDNA [clone 11] clone 1 isolated by the above method is depicted in [~~Figures~~ FIGS. 4-6] SEQ ID NO:1. --

Page 13, lines 15-29, delete in their entirety, and insert therefor

-- Subunits of TNF-R may be constructed by deleting terminal or internal residues or sequences. Particularly preferred sequences include those in which the transmembrane region and intracellular domain of TNF-R are deleted or substituted with hydrophilic residues to facilitate secretion of the receptor into the cell culture medium. The resulting protein is referred to as a soluble TNF-R molecule which retains its ability to bind TNF. A particularly preferred soluble TNF-R construct is TNF-RΔ235 (the sequence of amino acids 1-235 of [~~Figure~~ FIG. 2A] SEQ ID NO:1), which comprises the entire extracellular region of TNF-R, terminating with Asp^{235} immediately adjacent the transmembrane region.

Additional amino acids may be deleted from the [transmembrane] extracellular region while retaining TNF binding activity. For example, huTNF-RΔ183 which comprises the sequence of amino acids 1-183 of [~~Figure~~ Fig. 2A] SEQ ID NO:1, and TNF-RΔ163 which comprises the sequence of amino acids 1-163 of [Figure 2A] SEQ ID NO:1, retain the ability to bind TNF ligand as determined using the binding assays described below in Example 1. TNF-RΔ142, however, does not retain the ability to bind TNF ligand. This suggests that one or both of Cys^{157} and Cys^{163} is required for formation of an intramolecular disulfide bridge for the proper folding of TNF-R. Cys^{178}, which was deleted without any apparent adverse effect on the ability of the soluble TNF-R to bind TNF, does not appear to be essential for proper folding of TNF-R. Thus, any deletion C-terminal to Cys^{163} would be expected to result in a biologically active soluble TNF-R. The present invention contemplates such soluble TNF-R constructs corresponding to all or part of the extracellular region of TNF-R terminating with any amino acid after Cys^{163}. Other C-terminal deletions, such as TNF-FΔ157, may be made as a matter of convenience by cutting TNF-R cDNA with appropriate restriction enzymes and, if necessary, reconstructing specific sequences with synthetic oligonucleotide linkers. The resulting soluble TNF-R constructs are then inserted and expressed in appropriate expression vectors and assayed for the ability to bind TNF, as described in Example 1. Biologically active soluble TNF-Rs resulting from such constructions are also contemplated to be within the scope of the present invention. --

Page 14, lines 1-12, delete in their entirety.

Page 15, lines 10-21, delete in their entirety, and insert therefor

-- Both monovalent forms and polyvalent forms of TNF-R are useful in the compositions and methods of this invention. Polyvalent forms possess multiple TNF-R binding sites for TNF ligand. For example, a bivalent soluble TNF-R may consist of two tandem repeats of amino acids 1-235 of [~~Figure~~ FIG. 2A] SEQ ID NO:1, separated by a linker region. Alternate polyvalent forms may also be constructed, for example, by chemically coupling TNF-R to any clinically acceptable carrier molecule, a polymer selected from the group consisting of Ficoll, polyethylene glycol or dextran using conventional coupling techniques. Alternatively, TNF-R may be chemically coupled to biotin, and the biotin-TNF-R conjugate then allowed to bind to avidin, resulting in tetravalent avidin/biotin/TNF-R molecules. TNF-R may also be covalently coupled to dinitrophenol (DNP) or trinitrophenol (TNP) and the resulting conjugate precipitated with anti-DNP or anti-TNP-IgM, to form decameric conjugates with a valency of 10 for TNF-R binding sites. --

Page 30, lines 23-29, delete in their entirety, and insert therefor

-- A cDNA encoding a soluble huTNF-RΔ235 (having the sequence of amino acids 1-235 of [~~Figure~~ FIG. 2A] SEQ ID NO:1) was constructed by excising an 840 bp fragment from pCAV/NOT-TNF-R with the restriction enzymes Not1 and Pvu2. Not1 cuts at the multiple cloning site of pCAV/NOT-TNF-R and Pvu2 cuts within the TNF-R coding region 20 nucleotides 5' of the transmembrane region. In order to reconstruct the 3' end of the TNF-R sequences, two

oligonucleotides (encoding amino acids corresponding to Ala^{229}-Asp^{235} of SEQ ID NO:1) were synthesized and annealed to create the following oligonucleotide linker:

```
                Pvu2                        BamH1  Bgl2
CTGAAGGGAGCACTGGCGACTAAGGATCCA
GACTTCCCTCGTGACCGCTGATTCCTAGGTCTAG
AlaGluGlySerThrGlyAspEnd
```

This oligonucleotide linker has terminal Pvu2 and Bgl2 restriction sites, regenerates 20 nucleotides of the TNF-R, followed by a termination codon (underlined) and a BamH1 restriction site (for convenience in isolating the entire soluble TNF-R by Not1/BamH1 digestion). This oligonucleotide was then ligated with the 840 bp Not1/Pvu2 TNF-R insert into Bgl2/Not1 cut pCAV/NOT to yield psolhuTNF-RΔ235/CAVNOT, which was transfected into COS-7 cells as described above. This expression vector induced expression of soluble human TNF-R which was capable of binding TNF. --

Page 31, lines 1-12, delete in their entirety.

Page 31, lines 17-37, delete in their entirety, and insert therefor

-- A cDNA encoding a soluble huTNF-RΔ185 (having the sequence of amino acids 1-185 of [~~Figure~~ FIG. 2A] SEQ ID NO:1) was constructed by excising a 640 bp fragment from pCAV/NOT-TNF-R with the restriction enzymes Not1 and Bgl2. Not1 cuts at the multiple cloning site of pCAV/NO-TNF-R and Bgl2 cuts within the TNF-R coding region at nucleotide 637, which is 237 nucleotides 5' of the transmembrane region. The following oligonucleotide linkers

(encoding amino acids corresponding to Ile^{162}-Ala^{176} and Val^{177}-Arg^{185} of SEQ ID NO:1) were synthesized:

```
                Bgl2
5'-GATCTGTAACGTGGTGGCCATCCCTGGGAATGCAAGCATGGATGC-3'
     ACATTGCACCACCGGTAGGGACCCTTACGTTCG
  IleCysAsnValValAlaIleProGlyAsnAlaSerMetAspAla

                                              Not1
5'-       AGTCTGCACGTCCACGTCCCCCACCCGGTGAGC    -3'
  TACCTACGTCAGACGTGCAGGTGCAGGGGGTGGGCCACTCGCCGG
           ValCysThrSerThrSerProThrArgEnd
```

The above oligonucleotide linkers reconstruct the 3' end of the receptor molecule up to nucleotide 708, followed by a termination codon (underlined). These oligonucleotides were then ligated with the 640 bp Not1 TNF-R insert into Not1 cut pCAV/NOT to yield the expression vector psolTNFRΔ185/CAVNOT, which was transfected into COS-7 cells as described above. This expression vector induced expression of soluble human TNF-R which was capable of binding TNF. --

Page 32, lines 1-4, delete in their entirety.

Page 32, lines 9-25, delete in their entirety, and insert therefor

-- A cDNA encoding a soluble huTNF-RΔ163 (having the sequence of amino acids 1-163 of [~~Figure~~ FIG. 2A] SEQ ID NO:1) was constructed by excising a 640 bp fragment from pCAV/NOT-TNF-R with the restriction enzymes Not1 and Bgl2 as described in Example 4. The

following oligonucleotide linkers (encoding amino acids corresponding to Ile^{162}-Cys^{163} of SEQ ID NO:1) were synthesized:

```
          Bgl2          Not1
5'-GATCTGTTGAGC      -3'
     ACAACTCGCCGG
  IleCysEnd
```

This above oligonucleotide linker reconstructs the 3' end of the receptor molecule up to nucleotide 642 (amino acid 163), followed by a termination codon (underlined). This oligonucleotide was then ligated with the 640 bp Not1 TNF-R insert into Not1 cut pCAV/NOT to yield the expression vector psolTNFRΔ163/CAVNOT, which was transfected into COS-7 cells as described above. This expression vector induced expression of soluble human TNF-R which was capable of binding TNF in the binding assay described in Example 1. --

Page 32, lines 31-32, delete in their entirety, and insert therefor

-- A cDNA encoding a soluble huTNF-RΔ142 (having the sequence of amino acids 1-142 of [~~Figure~~ FIG. 2A] SEQ ID NO:1) was constructed by excising a 550 bp fragment from pCAV/NOT-TNF-R with the restriction enzymes Not1 and AlwN1. AlwN1 cuts within the TNF-R coding region at nucleotide 549. The following oligonucleotide

linker (encoding amino acids corresponding to Thr^{132}-Cys^{142} of SEQ ID NO:1) was synthesized:

Bgl2 Not1
5'-CTGAAACATCAGACGTGGTGTGCAAGCCCTGTTAAA-3'
CTTGACTTTGTAGTCTGCACCACACGTTCGGGACAATTTCTAGA
End

This above oligonucleotide linker reconstructs the 3' end of the receptor molecule up to nucleotide 579 (amino acid 142), followed by a termination codon (underlined). This oligonucleotide was then ligated with the 550 bp Not1/AlwN1 TNF-R insert into Not1/Bgl2 cut pCAV/NOT to yield the expression vector psolTNFRΔ142/CAVNOT, which was transfected into COS-7 cells as described above. This expression vector did not induced expression of soluble human TNF-R which was capable of binding TNF. It is believed that this particular construct failed to express biologically active TNF-R because one or more essential cysteine residue (e.g., Cys^{157} or Cys^{163}) required for intramolecular bonding (for formation of the proper tertiary structure of the TNF-R molecule) was eliminated. --

Page 33, lines 1-18, delete in their entirety.

Page 35, lines 28-29, delete in their entirety.

Page 36, lines 1-29, delete in their entirety, and insert therefor

-- A DNA fragment encoding TNF receptor and suitable for cloning into the yeast expression vector pIXY120 was first generated by polymerase chain reaction (PCR) amplification of the extracellular portion of the full length receptor from pCAV/NOT-TNF-R

(ATCC 68088). The following primers (encoding amino acids corresponding in part to amino acids Leu^{1}-Thr^{8} and Pro^{225}-Asp^{235} of SEQ ID NO:1) were used in this PCR amplification:

5' End Primer

5'-TTCCGGTACCTTTGGATAAAAGAGACTACAAGGAC
Asp718->ProLeuAspLysArgAspTyrLysAsp
GACGATGACAAGTTGCCCGCCCAGGTGGCATTTACA-3'
AspAspAspLys< ———— TNF-R ————>

3' End Primer (antisense)

5'-CCCGGGATCCTTAGTCGCCAGTGCTCCCTTCAGCTGGG-3'
BamH1>End<———————— TNF-R ———— >

The 5' end oligonucleotide primer used in the amplification included an Asp718 restriction site at its 5' end, followed by nucleotides encoding the 3' end of the yeast a-factor leader sequence (Pro-Leu-Asp-Lys-Arg) and those encoding the 8 amino acids of the FLAG® peptide (AspTyrLysAspAspAspAspLys) fused to sequence encoding the 5' end of the mature receptor. The FLAG® peptide (Hopp et al., *Bio/Technology* 6:1204, 1988) is a highly antigenic sequence which reversibly binds the monoclonal antibody M1 (ATCC HB 9259). The oligonucleotide used to generate the 3' end of the PCR-derived fragment is the *antisense* strand of DNA encoding sequences which terminate the open reading frame of the receptor after nucleotide 704 of the mature coding region (following the Asp residue preceding the transmembrane domain) by introducing a TAA stop codon (underlined). The stop codon is then followed by a BamH1 restriction site. The DNA sequences encoding

TNF-R are then amplified by PCR, substantially as described by Innis et al., eds., *PCR Protocols: A Guide to Methods and Applications* (Academic Press, 1990). --

Page 38, lines 22-29, delete in their entirety, and insert therefor

-- The murine cDNA library was amplified once and a total of 900,000 plaques were screened, substantially as described in Example 2, with the human TNF-R cDNA probe. Approximately 21 positive plaques were purified, and the Bluescript plasmids containing EcoR1-linkered inserts were excised (Stratagene, San Diego). Nucleic acid sequencing of a portion of murine TNF-R clone 11 indicated that the coding sequence of the murine TNF-R was approximately 88% homologous to the corresponding nucleotide sequence of human TNF-R. A partial nucleotide sequence of murine TNF-R cDNA clone 11 is set forth in [~~Figures~~ FIGS. 3A-3B] SEQ ID NO:3 and SEQ ID NO:4. --

Page 40, after line 2, insert

-- **DETAILED DESCRIPTION OF THE SEQUENCE LISTING**

SEQ ID NO:1 and SEQ ID NO:2 show the partial cDNA sequence and derived amino acid sequence of the human TNF-R clone 1. Nucleotides are numbered from the beginning of the 5' untranslated region. Amino acids are numbered from the beginning of the signal peptide sequence. The putative signal sequence is represented by amino acid -22 to -1. The N-terminus of the mature TNF-R begins with amino acid 1. The predicted transmembrane region extends from amino acids 236-265.

SEQ ID NO:3 and SEQ ID NO:4 show the cDNA sequence and derived amino acid sequence of murine TNF-R clone 11. The putative signal peptide sequence is represented by amino acids -22 to -1. The N-terminus of the mature TNF-R protein begins with amino acid 1. The predicted transmembrane region extends from amino acids 234 to 265. --

Page 41-53, please renumber as new pages 54-66, respectively.

IN THE CLAIMS:

Claim 18. (amended) An isolated DNA molecule encoding a protein comprising a sequence of amino acids selected from the group consisting of amino acids 1-163 of SEQ ID NO:1 and amino acids 1-233 of SEQ ID NO:3, wherein said protein is capable of binding TNF.

Claim 19. (amended) The isolated DNA molecule according to Claim 18, wherein said protein comprises amino acids 1-163 of SEQ ID NO:1.

Claim 20. (amended) The isolated DNA molecule according to Claim 18, wherein said protein comprises amino acids 1-185 of SEQ ID NO:1.

Claim 21. (amended) The isolated DNA molecule according to Claim 18, wherein said protein comprises amino acids 1-235 of SEQ ID NO:1.

Claim 22. (amended) An isolated DNA molecule encoding a protein selected from the group consisting of:

(a) a polypeptide having a sequence of amino acids comprising amino acids 1-163 of SEQ ID NO:1;

(b) a polypeptide having a sequence of amino acids comprising amino acids 1-233 of SEQ ID NO:3; and

(c) a polypeptide identical to the polypeptides of (a) or (b) except for one or more modification(s) to the sequence of amino acids selected from the group consisting of: (i) inactivated N-linked glycosylation sites; (ii) altered KEX2 protease cleavage sites; and (iii) substitution or deletion of cysteine residues,

wherein said protein is capable of binding TNF.

Claim 25. (amended) The host cell of Claim 24, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 26. (amended) The host cell of Claim 25, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 27. (amended) The host cell of Claim 26, wherein said mammalian cells are CHO cells.

Claim 29. (amended) The process of Claim 28, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 30. (amended) The process of Claim 29, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 31. (amended) The process of Claim 30, wherein said mammalian cells are CHO cells.

Claim 32. (amended) An isolated DNA molecule encoding a soluble TNF receptor protein comprising a sequence of amino acids selected from the group consisting of from about amino acid 1 to about amino acid 163 of SEQ ID NO:1 and from about amino acid 1 to about amino acid 233 of SEQ ID NO:3, wherein said soluble TNF receptor protein is capable of binding TNF protein.

Claim 33. (amended) The isolated DNA molecule according to Claim 32, wherein said soluble TNF receptor protein comprises from about amino acid 1 to about amino acid 163 of SEQ ID NO:1.

Claim 34. (amended) The isolated DNA molecule according to Claim 32, wherein said soluble TNF receptor protein comprises from about amino acid 1 to about amino acid 185 of SEQ ID NO:1.

Claim 35. (amended) The isolated DNA molecule according to Claim 32, wherein said TNF soluble receptor protein comprises from about amino acid 1 to about amino acid 235 of SEQ ID NO:1.

Claim 36. (amended) An isolated DNA molecule encoding a soluble TNF receptor protein selected from the group consisting of:

(a) a TNF receptor polypeptide having a sequence of amino acids comprising from about amino acid 1 to about amino acid 163 of SEQ ID NO:1;

(b) a TNF receptor polypeptide having a sequence of amino acids comprising from about amino acid 1 to about amino acid 233 of SEQ ID NO:3; and

(c) a TNF receptor polypeptide identical to the TNF receptor polypeptides of (a) or (b) except for one or more modification(s) to the sequence of amino acids selected from the group consisting of: (i) inactivated N-linked glycosylation sites; (ii) altered KEX2 protease cleavage sites; and (iii) substitution or deletion of cysteine residues,

wherein said soluble TNF receptor protein is capable of binding TNF.

Claim 39. (amended) The host cell of Claim 38, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 40. (amended) The host cell of Claim 39, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 41. (amended) The host cell of Claim 40, wherein said mammalian cells are CHO cells.

Claim 43. (amended) The process of Claim 42, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 44. (amended) The process of Claim 43, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 45. (amended) The process of Claim 44, wherein said mammalian cells are CHO cells.

Claim 46. (amended) An isolated DNA molecule encoding a soluble TNF receptor protein comprising a sequence of amino acids selected from the group consisting of from amino acid 1 to amino acid 163 of SEQ ID NO:1 and from amino acid 1 to amino acid 233 of SEQ ID NO:3, wherein said soluble TNF receptor protein is capable of binding TNF protein.

Claim 47. (amended) The isolated DNA molecule according to Claim 46, wherein said soluble TNF receptor protein comprises from amino acid 1 to amino acid 163 of SEQ ID NO:1.

Claim 48. (amended) The isolated DNA molecule according to Claim 46, wherein said soluble TNF receptor protein comprises from amino acid 1 to amino acid 185 of SEQ ID NO:1.

Claim 49. (amended) The isolated DNA molecule according to Claim 46, wherein said soluble TNF receptor protein comprises from amino acid 1 to amino acid 235 of SEQ ID NO:1.

Claim 50. (amended) An isolated DNA molecule encoding a soluble TNF receptor protein selected from the group consisting of:

(a) a TNF receptor polypeptide having a sequence of amino acids comprising from amino acid 1 to amino acid 163 of SEQ ID NO:1;

(b) a TNF receptor polypeptide having a sequence of amino acids comprising from amino acid 1 to amino acid 233 of SEQ ID NO:3; and

(c) a TNF receptor polypeptide identical to the TNF receptor polypeptides of (a) or (b) except for one or more modification(s) to the sequence of amino acids selected from the group consisting

of: (i) inactivated N-linked glycosylation sites; (ii) altered KEX2 protease cleavage sites; and (iii) substitution or deletion of cysteine residues,

wherein said soluble TNF receptor protein is capable of binding TNF.

Claim 53. (amended) The host cell of Claim 52, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 54. (amended) The host cell of Claim 53, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 55. (amended) The host cell of Claim 54, wherein said mammalian cells are CHO cells.

Claim 57. (amended) The process of Claim 56, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 58. (amended) The process of Claim 57, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 59. (amended) The process of Claim 58, wherein said mammalian cells are CHO cells.

Claim 60. (amended) An isolated DNA molecule encoding a protein comprising a sequence of amino acids selected from the group consisting of amino acids 1-163 of SEQ ID NO:1 and amino acids 1-233 of SEQ ID NO:3, wherein said protein lacks amino

acids 236-265 of SEQ ID NO:1 and amino acids 234-265 of SEQ ID NO:3, respectively, and wherein said protein is capable of binding TNF.

Claim 61. (amended) The isolated DNA molecule according to Claim 60, wherein said protein comprises amino acids 1-163 of SEQ ID NO:1.

Claim 62. (amended) The isolated DNA molecule according to Claim 60, wherein said protein comprises amino acids 1-185 of SEQ ID NO:1.

Claim 63. (amended) The isolated DNA molecule according to Claim 60, wherein said protein comprises amino acids 1-235 of SEQ ID NO:1.

Claim 64. (amended) An isolated DNA molecule encoding a protein selected from the group consisting of:

(a) a TNF receptor polypeptide having a sequence of amino acids comprising amino acids 1-163 of SEQ ID NO:1, wherein said polypeptide lacks amino acids 236-265 of SEQ ID NO:1;

(b) a TNF receptor polypeptide having a sequence of amino acids comprising amino acids 1-233 of SEQ ID NO:3, wherein said polypeptide lacks amino acids 234-265 of SEQ ID NO:3; and

(c) a TNF receptor polypeptide identical to the TNF receptor polypeptides of (a) or (b) except for one or more modification(s) to the sequence of amino acids selected from the group consisting of: (i) inactivated N-linked glycosylation sites; (ii) altered KEX2 protease cleavage

sites; and (iii) substitution or deletion of cysteine residues,

wherein said protein is capable of binding TNF.

Claim 67. (amended) The host cell of Claim 66, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 68. (amended) The host cell of Claim 67, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 69. (amended) The host cell of Claim 68, wherein said mammalian cells are CHO cells.

Claim 71. (amended) The process of Claim 70, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 72. (amended) The process of Claim 71, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 73. (amended) The process of Claim 72, wherein said mammalian cells are CHO cells.

Claim 74. (amended) An isolated DNA molecule encoding a protein comprising a sequence of amino acids selected from the group consisting of amino acids 1-163 of SEQ ID NO:1 and amino acids 1-233 of SEQ ID NO:3, wherein said protein lacks a functional transmembrane region, and wherein said protein is capable of binding TNF.

Claim 75. (amended) The isolated DNA molecule according to Claim 74, wherein said protein comprises amino acids 1-163 of SEQ ID NO:1.

Claim 76. (amended) The isolated DNA molecule according to Claim 74, wherein said protein comprises amino acids 1-185 of SEQ ID NO:1.

Claim 77. (amended) The isolated DNA molecule according to Claim 74, wherein said protein comprises amino acids 1-235 of SEQ ID NO:1.

Claim 78. (amended) An isolated DNA molecule encoding a protein selected from the group consisting of:

(a) a TNF receptor polypeptide having a sequence of amino acids comprising amino acids 1-163 of SEQ ID NO:1;

(b) a TNF receptor polypeptide having a sequence of amino acids comprising amino acids 1-233 of SEQ ID NO:3; and

(c) a TNF receptor polypeptide identical to the TNF receptor polypeptides of (a) or (b) except for one or more modification(s) to the sequence of amino acids selected from the group consisting of: (i) inactivated N-linked glycosylation sites; (ii) altered KEX2 protease cleavage sites; and (iii) substitution or deletion of cysteine residues,

wherein said protein lacks a functional transmembrane region; and wherein said protein is capable of binding TNF.

Claim 81. (amended) The host cell of Claim 80, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 82. (amended) The host cell of Claim 81, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 83. (amended) The host cell of Claim 82, wherein said mammalian cells are CHO cells.

Claim 85. (amended) The process of Claim 84, wherein said host cell is selected from the group consisting of microbial cells and mammalian cells.

Claim 86. (amended) The process of Claim 85, wherein said mammalian cells are selected from the group consisting of L cells, C127 cells, 3T3 cells, CHO cells, BHK cells and COS-7 cells.

Claim 87. (amended) The process of Claim 86, wherein said mammalian cells are CHO cells.

REMARKS

The specification is being amended in a manner consistent with 37 C.F.R. § 1.121(b)(1)(iii) as requested by the Examiner in a teleconference on April 16, 1999.

The above-noted amendments to the specification are identical to those previously submitted in the Preliminary Amendment filed October 9, 1998, which the Examiner has advised he has not entered because they were not made in accordance with